POTASSIUM BROMATE

Document History
Published: 1985
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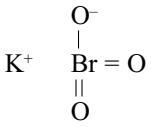
I. IDENTIFICATION

Chemical Name: Potassium bromate
Synonyms: Bromic acid, potassium salt
CAS Number: 7758–01–2
Molecular Formula: $KBrO_3$
Structural formula:



DOT: UN1484

II. CHEMICAL AND PHYSICAL PROPERTIES[1]

Physical State: White solid
Molecular Weight: 167.00
Conversion Factors: ppm to mg/m^3 — not applicable
Melting Point: 350°C (662°F) with decomposition
Boiling Point: not applicable
Vapor Pressure: not available
Saturated Vapor Concentration: not available
Odor Description and Threshold: not available
Flammability Limits: not applicable
Flash Point: not applicable
Autoignition Temperature: not applicable
Specific Gravity: 3.34, temp unspecified
Solubility in Water: 7.53% by weight at 25°C (77°F)
Stability: Oxidizer
Reactivity and Incompatibilities: Oxidizer, reacts violently with reducing agents

III. USES

Used in flour milling industries as additive to improve baking properties, as an oxidizing agent, analytical chemistry reagent, and in home permanent-wave neutralizing products.

IV. ANIMAL TOXICITY DATA

A. Acute Toxicity and Irritancy

1. Oral

Rats – LD_{50} 321 mg/kg[1]
Mice – LD_{50} 289 mg/kg[1]

2. Eye

Rabbit – Slight initial pain and irritation. Slight temporary corneal injury which resolved in 7 days.[2]
Rabbit – Moderate irritation with almost complete recovery in 48 hours.[3]

3. Skin

a. Toxicity

Rabbit – Dose not reported. Wet solid is slowly absorbed through intact skin in toxic amounts.[4]
Guinea Pig – LD_0 >1.0 g/kg. No deaths, highest dose animal lost weight during 2 week observation, others gained weight normally.[3]

b. Irritation

Rabbits – Dry material is slightly irritating; damp material is moderately irritating and may cause a burn if contact is prolonged.[4]
Guinea Pig – Moist material caused slight irritation after 24 hour contact.[3]

4. Inhalation

No data available.

5. Intraperitoneal Injection

Rats LD_{50} 50–100 mg/kg[3]
Mice LD_{50} 177 mg/kg[1]

B. Subacute Toxicity

No data available.

C. Subchronic Toxicity

Male and female rats (10 per sex) were treated with potassium bromate in the drinking water at 150, 300, 600, 1250, 2500, 5000, and 10,000 ppm for 13 weeks.[5] All rats in dose groups of greater than 1250 ppm (about 171 mg/kg) died. Toxicity observed included inhibition of body weight gain in males and increase in serum parameters in both sexes at 600 ppm (77 mg/kg and above). Histological changes in renal tubules were observed.

In male rats treated with $KBrO_3$ at a single dose level of about 40 mg $KBrO_3$/kg/day in the drinking water for 15 months, kidney tubule changes with increased BUN and decreased body weight gain were observed.[6]

D. Chronic Toxicity and Carcinogenicity

Several long term studies have reported the carcinogenic effects of $KBrO_3$.[7-9] The results across studies report consistent findings in rats with statistically significant increases in kidney cell tumors, thyroid follicular tumors and peritoneal mesotheliomas observed, some as early as 13 weeks.[7] Renal cell tumors were also found in mice.[9]

Rats (Fisher 344, 52/sex/group) were dosed with 250 or 500 ppm (12.5 or 27.7 mg/kg/day) $KBrO_3$ in drinking water for 110 weeks.[7] A decrease in body weight gain and survival occurred in males receiving 500 ppm with a mean survival time of 88 weeks. A high incidence (>50%) of renal cell tumors, classified as adenomas and adenocarcinomas, in both sexes at both 250 and 500 ppm were observed. Mesotheliomas (28/59) were significantly increased in males at 500 ppm.

In another study, F344/N male rats (50 per group) were treated with $KBrO_3$ in the drinking water at 20, 100, 200 or 400 ppm for up to 100 weeks, delivering doses of 0, 1.5, 7.9, 16.9, and 37.5 mg/kg.[9] Decreased survival was observed in the 200 ppm and 400 ppm groups. Decreased body weight gain and decreased body weight were observed in the high dose group. A dose-dependent increased incidence of mesotheliomas (27/63 at 400 ppm) was reported at 100 ppm and above. Rats treated with 400 ppm had an increase in renal cell tumors. Rats treated with 200 ppm or more had an increased incidence of thyroid follicular tumors.

$B6C3F_1$ male mice (50 per group) were treated with 0, 0.08, 0.4, or 0.8 g/L (9.1, 42.4, or 78 mg/kg/d, respectively) $KBrO_3$ in the drinking water for up to 100 weeks.[9] Survival and body weight gain were not affected by treatment. The high dose group had significantly lowered water consumption. The authors reported an increase in renal cell tumors as biologically significant though it was not dose-related. The tumor incidence was significantly increased ($p<0.05$) at the low dose (0.08 g/L) compared to controls.

When female $B6C3F_1$ mice were given potassium bromate at doses of 500 or 1000 ppm for 78 weeks, no significant differences in tumor incidences between experimental and control groups were apparent.[9]

Non-neoplastic lesions observed in long-term studies in male and female rats include hyperplasia of the kidney tissue.[7,9] No non-carcinogenic effects were found in male mice. Non-carcinogenic effects were not reported in female mice.[8] The only NOEL for non-cancer endpoints is identified by DeAngelo. There was a dose-related increase in hyperplasia of urothelial lining of the renal pelvis observed at 7.9 mg bromate/kg and above. The NOEL for non-neoplastic lesions is 1.5 mg/kg.

Feeding studies in rats using bread made from flour bleached with $KBrO_3$ showed no adverse effects[10]; however, the level of ingested bromate ion is presumed to be very low due to its reduction to bromide during the bleaching and baking process.

E. Developmental / Reproductive Toxicity

No data was located on the reproductive toxicity of $KBrO_3$. A study of the sodium salt has been conducted.[11] Female rats (gestational exposure, 13 per group) were dosed with $NaBrO_3$ in the water on gestation Day 6 through parturition at doses of 0, 25, 80, or 250 ppm. Males (10 per group) were treated on Days 6–34/35 of the study with a resulting calculated intake of sodium bromate estimated at 2, 6.5, and 19 mg/kg/d, respectively. A second group of females (peri-conception exposure, n=10) were treated from Study Day 1 until necropsy (Study Day=34). The treated males were mated with this second group of treated females from Study Day 13–18. No effects on fertility were observed, but in males a dose-related decrease in sperm density was statistically significant by trend test ($p=0.007$) and at 250 ppm (16.3 mg BrO_3^-/kg) ($p<0.05$). No effects on

female reproductive function were observed. No developmental effects were observed in pups sacrificed at postnatal Day 5, but necropsies were not performed. The authors reported a NOEL of 80 ppm (5.6 mg BrO_3^-/kg) based on a statistically significant 18% reduction in epididymal sperm count at the highest dose, although the reduction at the reported NOEL was 14%.

F Genotoxicity

Results were negative when tested on *Salmonella typhimurium* strains TA1535, TA1537, TA1538, and *Saccharomyces cerevisiae*, strain D4 in *in vitro* microbial assays with and without metabolic activation.[12] TA98 plus S-9 mixture and TA100 gave negative results, but with TA100 plus S-9 mixture positive results were obtained.[13] Potassium bromate is positive in the mouse micronucleus test on examination of bone marrow cells[14] and peripheral blood cells.[15,16] It is positive in the chromosomal aberration assay *in vitro* in Chinese hamster fibroblasts,[13] the cytogenetic assay on rat bone marrow cells *in vivo*,[17] and in the alkaline comet assay.[18] Potassium bromate induced gene mutations at the HPRT locus and induced oxidative DNA damage with significant increases in levels of 8-oxodeoxyguanosine.[18]

G. Metabolism and Pharmacokinetics

Bromate is absorbed and is found in plasma and urine. Bromate was not detected in tissues but increased bromide levels were observed following oral dosing.[19] Glutathione facilitates the reduction of bromate to bromide.[20] Excretion is mainly in the urine.

H. Other

Subcutaneous injections of $KBrO_3$ (50 mg/kg) daily for 2 weeks in guinea pigs caused peripheral auditory nerve damage with apparent hearing loss.[21]

Guinea pigs (no data available on sex or number of animals) were given 10–20 mg/kg by intraperitoneal injection for 10–20 days (100–400 mg/kg total). A high incidence of death was reported. Histological examination revealed severe damage to the kidney tubule system. Degeneration of the cochlear sensory cells was also observed.[22]

Based on the tumor incidence data from the DeAngelo study and using a linear low-dose extrapolation methodology, the Environmental Protection Agency[23] calculated a cancer risk estimate for oral exposure to bromate. There are significant uncertainties in using this oral cancer potency estimate for assessing occupational cancer risk, and therefore it is not used as the quantitative basis for deriving the OEL. However, as a qualitative comparison, the proposed OEL value of 0.1 mg/m^3 is within the same concentration range (roughly 3-fold greater) than the concentration that corresponds to a 1:1000 risk level calculated from EPA's oral cancer potency estimate.

V. HUMAN USE AND EXPERIENCE

A. Use in Flour

Potassium bromate is added to some flour at levels not exceeding 50 ppm by weight. Bromate is converted to bromide in the baking process.

B. Poisoning in Humans

Several cases of serious or fatal poisonings have been reported from ingestion of permanent wave neutralizer containing potassium bromate. Symptoms included gastrointestinal effects, transient restlessness followed by apathy, possible methemoglobin formation and hemolysis, and acute renal failure. Autopsies revealed effects on the kidney, liver and brain.[24-27] Loss of hearing has also been reported following ingestion of bromate, 0.5–40 grams, either as the sodium or potassium salt. The onset of deafness occurred within 4–16 hours following ingestion, and was severe, sensorineural and irreversible.[26]

VI. RATIONALE

Potasium bromate is moderately toxic orally and irritating to skin and eyes. High doses of potassium bromate can cause loss of hearing and kidney damage. Following long-term dosing in animals, there was an increased tumor incidence of mesotheliomas, renal cell tumors and thyroid follicular tumors. Hyperplasia of the kidney was the only non-carcinogenic lesion reported in chronic studies. The NOEL for the kidney hyperplasia was identified at 1.5 mg $KBrO_3$/kg/day. Limited data on an analogous bromate salt suggests that this level would be protective for reproductive and developmental effects.

This material is likely to be an irritant, but no inhalation data are available to determine the threshold for this response. The proposed OEL is based on extrapolation from oral toxicity for systemic effects, and the absence of irritation data is a key area of uncertainty. The OEL guide of 0.1 mg/m^3 should provide adequate protection from kidney damage, hearing loss, and non-cancer endpoints and provide an acceptable risk for cancer endpoints.

VII. RECOMMENDED OEL

8-hr time-weighted average (TWA): 0.1 mg/m^3

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